

Health Advisory:

Increase in Reported Cases of Tick-Borne Rickettsial Diseases

June 14, 2007

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The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

Health Alerts convey information of the highest level of importance which warrants immediate action or attention from Missouri health providers, emergency responders, public health agencies, and/or the public.

Health Advisories provide important information for a specific incident or situation, including that impacting neighboring states; may not require immediate action.

Health Guidances contain comprehensive information pertaining to a particular disease or condition, and include recommendations, guidelines, etc. endorsed by DHSS.

Health Updates provide new or updated information on an incident or situation; can also provide information to update a previously sent Health Alert, Health Advisory, or Health Guidance; unlikely to require immediate action.

Health Advisory
June 14, 2007

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SUBJECT: Increase in Reported Cases of Tick-Borne Rickettsial
Diseases in Missouri in 2007

SUMMARY

- From January 1 to June 1, 2007, cases of suspected and confirmed tick-borne rickettsial diseases (TBRDs), including ehrlichiosis/anaplasmosis and Rocky Mountain spotted fever (RMSF), have increased in Missouri compared to the previous five years.
- Health-care providers should be aware of the signs and symptoms of these diseases, which include fever, headache, malaise, and rash. Rash is much more common in RMSF (90%) compared with ehrlichiosis/anaplasmosis (<10%-60%).
- Treatment should begin without delay.
- Adults-100 mg per dose administered twice daily (orally or intravenously)
- Children- 2.2 mg/kg body weight per dose administered twice daily (orally or intravenously) to a maximum of 100 mg/dose
- Confirmatory testing, including polymerase chain reaction (PCR) and/or paired acute and convalescent serology can be obtained through the Missouri State Public Health Laboratory (MSPHL) at (573) 751-0633, or through the St. Louis Children's Hospital Virology Laboratory (PCR only) at 314-454-4161.
- TBRD should be suspected in anyone with symptoms as described above and a history of tick bite or spending time in a tick habitat (grassy or wooded area). Eliciting a history of possible tick exposure is critical to making the diagnosis. Suspect cases or positive laboratory results should be reported to the local public health agency, or the Missouri Department of Health and Senior Services (DHSS) at 573-751-6113.
- Primary prevention includes avoidance of tick habitats, the use of DEET-containing repellents, wearing long-sleeve shirts and pants, and thoroughly checking for and removing ticks promptly.
- Detailed information on the clinical presentation, diagnosis, treatment, and prevention of TBRDs is available from the Centers for Disease Control and Prevention (CDC) at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm>.

INTRODUCTION

This Health Advisory is being issued following confirmation of a tick-borne disease-related fatality in a Missouri citizen. A northeast Missouri child died May 23, 2007. Diagnostic tests performed at St. Louis Children's Hospital indicate the child was infected with *Ehrlichia chaffeensis*, a tick-borne rickettsia that causes human monocytic ehrlichiosis (HME). Missouri Department of Health and Senior Services (DHSS) and local public health disease investigators found that the child had been hospitalized with symptoms consistent with ehrlichiosis after apparently being bitten by a tick. The child died about ten days after symptoms initially appeared despite intensive medical care.

Ehrlichiosis/anaplasmosis, like Rocky Mountain spotted fever (RMSF), another tick-borne rickettsial disease (TBRD), can be life threatening. The early signs and symptoms of both

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diseases are notoriously nonspecific and may appear to be a benign viral illness, making diagnosis very difficult. Because TBRD can be severe, especially if untreated, health care practitioners should not delay treatment when there is a strong suspicion of a rickettsial illness.

BACKGROUND

Ehrlichiosis/anaplasmosis and RMSF are endemic in Missouri with case reports typically increasing during the warmer months. The causative agents of TBRD in the U.S. include:

- *Ehrlichia chaffeensis*– (HME)
- *Ehrlichia ewingii*– (Human granulocytic ehrlichiosis [HGE])
- *Anaplasma phagocytophilum* (formerly *E. phagocytophilum*)– (Human granulocytic anaplasmosis [HGA])
- *Rickettsia rickettsiae*– RMSF

DHSS has received increased reports in 2007 of several TBRD, including ehrlichiosis/anaplasmosis and RMSF. Provisional data showed that 16 cases of ehrlichiosis have been officially reported from January 1 to June 1, 2007, compared to an average of nine cases per year for the same periods of the past five years. In addition, 54 cases of RMSF have been reported from January 1 to June 1, 2007, compared to an average of 22 cases per year for the same periods of the past five years. Other, non-rickettsial, tick-borne diseases reported in Missouri in 2007 include two cases of **tularemia** and 10 cases of **Lyme-like disease**. (Some of these reported cases are still under investigation or in various stages of testing.)

CLINICAL MANIFESTATIONS

Ehrlichiosis/anaplasmosis is characterized by acute onset of fever, headache, myalgia, and malaise. Nausea, vomiting, and rash may be present in some cases. A rash with variable distribution occurs in 60% of children and 25% of adults with HME. Rash is less common with HGA (approximately 10% of cases). For both HME and HGE/HGA, the onset of rash is typically about one week after onset of other symptoms.¹ Laboratory findings may include thrombocytopenia, leukopenia, and/or elevated liver enzymes. Severe manifestations of the disease may include prolonged fever, renal failure, disseminated intravascular coagulopathy, meningoencephalitis, adult respiratory distress syndrome, seizures, and/or coma. An estimated 2%-3% of ehrlichiosis patients die from the infection. Immunocompromised individuals are at higher risk of severe disease and death. Included here would be those with compromised immune systems caused by end-stage renal disease, cancer, HIV/AIDS, transplant, or splenectomy, as well as in those taking immunocompromising medications such as steroids, anti-rheumatologic agents, transplant anti-rejection agents, or cancer chemotherapy.

In **Rocky Mountain spotted fever** the initial presenting symptoms are the same as for HME. The rash of RMSF occurs in about 90% of cases and it occurs sooner in the course of the illness, usually 2-4 days after onset of fever. The rash is typically a maculopapular rash beginning on the wrists and ankles. Eventually, the rash spreads to almost the entire body, including the palms and soles, but sparing the face, and becomes petechial in character. Early laboratory findings (CBC, chemistry panel) are similar to those seen with ehrlichiosis/anaplasmosis.

TBRD should be suspected in patients experiencing illness as described above following a tick bite or known exposure to grassy or wooded areas where ticks are abundant (since many cases occur in individuals who do not recall being bitten by a tick).

DIAGNOSTIC TESTING

A complete blood cell count (CBC), comprehensive metabolic panel, and examination of peripheral blood smear (which may show intracellular inclusions known as morulae in ehrlichiosis/anaplasmosis) are essential when considering a diagnosis of TBRD to assess for leukopenia, thrombocytopenia, hyponatremia or elevation

of liver enzymes.² Rapid confirmatory assays are not available to guide treatment decisions of acutely ill patients. Polymerase chain reaction (PCR) is highly sensitive for TBRD. There is no optimal timing for obtaining samples for PCR, but obtaining laboratory specimens as early as possible in the course of disease, preferably before therapy has started, will increase the probability of an accurate result. Serology by immunofluorescence assay (IFA) of sequential acute and convalescent samples confirms an active infection. The sensitivity of the IFA depends on the timing of sample collection. The first sample should be taken within the first week after onset of illness. The second sample should be drawn 2-3 weeks later.² In addition to providing a definitive diagnosis to the clinician, laboratory confirmation of infection is also vital to understanding the epidemiology and public health impact of TBRD.

The following diagnostic tests are recommended when TBRD is suspected:

- A complete blood cell count (CBC), comprehensive metabolic panel, and examination of the peripheral blood smear (which may show intracellular inclusions known as morulae in HME/HGA) are essential when considering a diagnosis of TBRD.²
- AND
- Nucleic acid detection by PCR (EDTA/purple-top tube blood sent on freeze packs)
- OR
- Serological testing via IFA to demonstrate seroconversion (red-top tube, acute and convalescent sera, 2-3 weeks apart). Single serological results are of limited clinical or epidemiologic value.
- OR
- Immunohistochemistry from biopsy or autopsy specimens. This is particularly useful for diagnosing patients from whom no or only a single acute IFA serology can be obtained.

The Missouri State Public Health Laboratory (MSPHL) does not test for rickettsial diseases. However, MSPHL will submit paired serum specimens, whole blood, and biopsy materials to the Centers for Disease Control and Prevention (CDC) for testing. No fees are assessed for specimens sent to CDC through MSPHL. To contact MSPHL about submitting specimens, call (573) 751-0633.

St. Louis Children's Hospital Virology Laboratory will accept specimens for ehrlichia/anaplasma PCR testing. Submissions must include the submitting physician's written order requesting testing and insurance billing information for the patient. For more information, call (314) 454-4161. (Note that Children's Hospital Virology Laboratory does not do PCR for RMSF.)

TREATMENT

Doxycycline is the drug of choice for treatment of TBRD in adults and children². Treatment should not be delayed in order to obtain laboratory tests or test results.

- Adults: 100 mg per dose administered twice daily (orally or intravenously)
- Children: 2.2 mg/kg body weight per dose administered twice daily (orally or intravenously) for children weighing <100 lbs. (45.4 kg) (maximum 100 mg/dose)²
- Duration: Treatment should continue for at least three days after the fever subsides and until evidence of clinical improvement is noted (typical total course of 5-10 days¹). Severe or complicated disease might require a longer treatment course.
- Prophylaxis: There is **no** role for prophylactic antibiotics following a tick bite in asymptomatic individuals.¹ However, immunocompromised individuals, who are at higher risk for severe disease, should monitor themselves for early symptoms of illness.

Note: Despite concerns regarding dental staining with tetracycline-class antimicrobial agents in young children, doxycycline provides superior therapy for this potentially life-threatening disease. Available data suggest that courses of doxycycline ≤ 14 days do not cause significant discoloration of permanent teeth.¹

PREVENTION

The best method for preventing TBRD is to avoid exposure to vector ticks. If exposure is unavoidable, measures recommended to reduce the risk of infection include:

- Keeping ticks off the skin –
 - Protective clothing – long-sleeved shirts and long pants
 - Tick repellents that contain DEET
- Performing tick checks –
 - Checking the entire body for ticks daily
 - Prompt removal of attached ticks – preferably with tweezers

The American Academy of Pediatrics (AAP) has stated that insect repellents containing DEET are most effective against ticks. Thirty percent DEET is the maximum amount currently recommended by the AAP for children two months of age or older. DEET should not be used on infants under 2 months of age.

REPORTING

All TBRD are reportable conditions in the State of Missouri. Health care providers should contact their local public health agency as soon as possible to aid in the public health investigation of TBRD cases.

ADDITIONAL INFORMATION

More detailed information from CDC on the clinical presentation, diagnosis, treatment, and prevention of TBRDs is published in a 2006 issue of *MMWR Recommendations and Reports*, available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm>. Continuing education credits (CME, CEU, and CNE) in conjunction with this report are available through March 31, 2008.

MSPHL does not accept ticks for identification or testing. The University of Missouri Extension Service Plant Diagnostic Clinic will identify physical samples or digital images of ticks for a \$15 fee. (Submission instructions and forms are available at <http://soilplantlab.missouri.edu/plant/>). Testing of ticks for tick-borne infectious agents is not recommended except in research studies.

Any questions should be directed to DHSS's Bureau of Communicable Disease Control and Prevention at (573) 751-6113 or (866) 628-9891.

REFERENCES

1. American Academy of Pediatrics. Ehrlichia and Anaplasma Infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2006.
2. Centers for Disease Control and Prevention. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichiosis, and anaplasmosis-United States: a practical guide for physicians and other health care and public health professionals. *MMWR* 2006; 55(No. RR-4).